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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/598,736	07/19/2007	Sophie Lotersztajn	26600	9624

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EXAMINER	
BORI, IBRAHIM D	

ART UNIT	PAPER NUMBER
1629	

NOTIFICATION DATE	DELIVERY MODE
07/08/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

sanofi_docketing@ssmp.com
betty@ssmp.com

Office Action Summary	Application No.	Applicant(s)	
	10/598,736	LOTERSZTAJN ET AL.	
	Examiner	Art Unit	
	IBRAHIM D. BORI	1629	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 April 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28,29 and 32-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28,29 and 32-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *December 9, 2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Reassignment of Application

Please note that this application has been reassigned to Examiner Ibrahim Bori, in Art Unit 1629. In order to expedite accurate processing of the application papers, all future correspondence with the office should reflect this change.

Information Disclosure Statement

The information disclosure statements (IDS) submitted on December 9, 2006 has been considered by the Examiner. The submissions are in compliance with the provisions of 37 CFR § 1.97. Enclosed with this Office Action is a return-copy of the Form PTO-1449 with the Examiner's initials and signature indicating those references that have been considered.

Status of the Application

The Instant Application claims benefit of European Application No. 04290633.9, filed on March 9, 2004, and is a national stage entry of PCT/EP2005/003285, filed on August 8, 2005.

Claims 28, 29 and 32-37 are pending and are the subject of this Office Action.

Applicants' Amendment and Response to the Office Action dated November 29, 2010, filed on April 29, 2011 are acknowledged and entered.

Applicants' amendment to claim 29 to place the claim in proper dependent form is acknowledged and entered. Accordingly, objection to claim 29 is withdrawn.

Applicants' amendment to claim 32 to correct the inadvertent typographical error is acknowledged and entered. Accordingly, objection to claim 32 is withdrawn.

Applicants' amendment to the specification to reflect the proper sequence identification numbers, (SEQ ID), at the appropriate location in the specification, and the submission of a substitute copy of the sequence listing in accordance with 37 CFR 1.82(g), is acknowledged and entered. Accordingly, objection to the specification is withdrawn.

Applicants' arguments that the secondary reference used in the previous objection was not a relevant art because the art was published after the priority date of the Instant Application (i.e. March 9, 2004) is deemed to be persuasive. Rejections and /or objections not reiterated from previous Office Actions are hereby withdrawn. The rejections set forth herein constitute the complete set of rejection being applied to the Instant Application presently.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

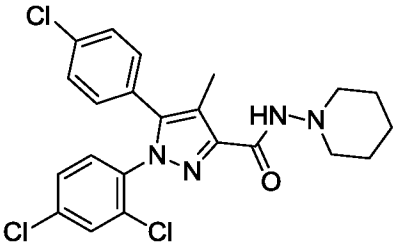
The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 28, 29 and 32-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Nature Medicine,* ***2001,*** 7(7), 827-832, to Batkai et al (hereafter 'Batkai' cited by Applicants and submitted by Applicants in the instant application), in view of US 5,624,941, to Barth et al (hereinafter 'Barth', cited by Applicants) and US 6,143,752, to Oren (hereinafter 'Oren').

The Claimed Invention

The claimed invention is drawn to a method of treating hepatic fibrosis in mammal comprising the administration of a therapeutic amount of at least one selective central cannabinoid-1 (CB1) receptor antagonist, wherein the CB1 receptor antagonist is a pyrazole derivative known by those skilled in the art, and exemplified by the compound of the formula shown below (see figure 1), or a pharmaceutically acceptable salt thereof.



5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-*N*-(piperidin-1-yl)-1*H*-pyrazole-3-carboxamide

SR141716

CAS 168273-06

Figure 1. CB1 receptor antagonist

What the Art Teaches

Batkai discloses a method of treating liver cirrhosis comprising the administration of a (CB1) receptor antagonist such as SR141716 also known by those skilled in the art as SR141716A, N-piperidino-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methylpyrazole-3-carboxamide or 5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-N-(piperidin-yl)-1*H*-pyrazole-3-carboxamide. According to Batkai's teachings, cirrhotic patients are endotoxemic, and activation of vascular cannabinoid CB1 receptors has been implicated in endotoxin-induced hypotension. Batkai further discloses that: "*compared to with non-cirrhotic controls, in cirrhotic human livers there was a three fold increase in CB1 receptor on isolated vascular endothelia cells".* See abstract.

However, Batkai does not disclose a method of treating hepatic fibrosis comprising the administration of SR141716A as required by the claimed invention.

According to the teachings of Oren: "*In the case of the liver, the end-stage of fibrosis is cirrhosis. Pathologically, cirrhosis is defined as extensive fibrosis in the liver".* See column 1, lines 41-43.

The disclosures of Batkai and Oren combined to address claims 28, 29 and 32 of the Instant Application.

Barth discloses pyrazole derivatives of the exact structural depiction as shown in claim 29 of the Instant Application. Bart further teaches that the disclosed pyrazole derivatives exemplified by SR141716A have a good affinity for cannabinoid receptor and are therefore particularly valuable in the therapeutic areas in which cannabis is

known to be involved. See column 1, lines 23-26, column 2, structure (I), column 80, example 211. According to Barth's disclosure, the pyrazole compounds and their pharmaceutically acceptable salts can be used in humans at daily doses that can preferably vary from 0.5 to 400 mg, more particularly from 2.0 to 1000 mg depending on the age of the subject to be treated or the type of treatment. See column 27, lines 8-15.

The teachings of Batkai, Oren, and Barth combine to address claims 28, 29 and 32-34.

Notably, claims 35-37 are also rejected in the Instant application because in assigning the claims their broadest reasonable interpretation, the language “a portion of” is construed as one amino acid and the same is present in all of the sequences and the presence of G-coupled receptors understood to be ubiquitous. Regarding percentage homology, it is well understood in the art that the same would be discoverable as an effective percentage using random optimization for the desired/intended effect.

Therefore, one of ordinary skill in the art would have had a reasonable expectation of success in arriving at the invention as claimed because each of Batkai, Oren and Barth are directed toward a method of treating hepatic fibrosis comprising the administration of a therapeutically effective amount a CB1 receptor antagonist such as 5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-N-(piperidin-yl)-1*H*-pyrazole-3-carboxamide encompassed by the claimed invention. A skilled artisan would have also been motivated by the need to treat human liver diseases. One of ordinary skill in the art

would have been additionally motivated by the need to ameliorate the economic and psychological toll of human liver diseases.

MPEP §2144.06 states "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (citations omitted) (Claims to a process of preparing a spray-dried detergent by mixing together two conventional spray-dried detergents were held to be prima facie obvious.). See also In re Crockett, 279 F.2d 274, 126 USPQ 186 (CCPA 1960) (Claims directed to a method and material for treating cast iron using a mixture comprising calcium carbide and magnesium oxide were held unpatentable over prior art disclosures that the aforementioned components individually promote the formation of a nodular structure in cast iron.); and Ex parte Quadranti, 25 USPQ2d 1071 (Bd. Pat. App. & Inter. 1992) (mixture of two known herbicides held prima facie obvious)".

Therefore, since each of the references teach administering 5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-N-(piperidin-yl)-1*H*-pyrazole-3-carboxamide to treat therapeutic areas in which cannabis is known to be involved, combining them flows logically from their having been taught in prior art.

Correction of Inventorship

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Conclusions

No claim is allowable.

If Applicants should amend the claims, a complete and responsive reply will clearly identify where support can be found in the disclosure for each amendment. Applicants should point to the page and line numbers of the application corresponding to each amendment, and provide any statements that might help to identify support for the claimed invention (e.g., if the amendment is not supported in *ipsis verbis,* clarification on the record may be helpful). Should the Applicants present new claims, Applicants should clearly identify where support can be found in the disclosure.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to IBRAHIM D. BORI whose telephone number is (571)270-7020. The examiner can normally be reached on Monday through Friday 8:00AM-5:00PM(EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, JEFFREY S. LUNDGREN can be reached on 571-272-5541. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/IBRAHIM D BORI/
Examiner, Art Unit 1629

/Jeffrey S. Lundgren/
Supervisory Patent Examiner, Art Unit 1629